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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,461	03/02/2001	Esteban Cvitkovich	13566.105002	9636

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
11/09/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

usptomailnyc@kslaw.com

Office Action Summary	Application No.	Applicant(s)	
	09/787,461	CVITKOVICH ET AL.	
	Examiner	Art Unit	
	Phyllis G. Spivack	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-17 and 24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12-17 and 24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-16-07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicants' Amendment filed August 3, 2007 is acknowledged. Claims 12-17 and 24-35 remain under consideration.

An Information Disclosure Statement filed July 16, 2007 is further acknowledged and has been reviewed to the extent each reference was provided.

A Declaration of Jose Jimeno under 35 U.S.C. § 1.131 filed August 3, 2007 is further acknowledged.

The disclosure is objected to for the following informality: At the first occurrence of an acronym, it is customary to spell out the compound contemplated. Specifically, for Et-743, Ecteinascidin-743 should be recited at its first occurrence in the independent claim.

Appropriate correction is required.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: There is no antecedent basis in the specification for the recitations "at intervals of **about** 1-6 weeks," "**about** 2 to **about** 24 hours" in claim 12 and "**about** 1000 to **about** 1650 micrograms/m^2" in claim 15.

Applicants are urged to review the claims for proper antecedent basis for all recitations where a range or dosage is recited and preceded by the term "about."

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession

of the claimed invention. Applicants refer to page 12, lines 1-3, for support of the amendment to claim 14, wherein "about 1 week" has been changed to "about 3 to 4 weeks." The citation on page 12 recites "3-4 weeks." See *In re Rasmussen*, 211 USPQ 323 (CCPA 1981).

In the last Office Action it was asserted Applicants have claimed benefit of prior-filed, non-US patent applications:

GB 9911183.3, filed on 13 May 1999

GB 9911346.6, filed 14 May 1999

GB 9927005.0, filed 15 November 1999

GB 9918534.0, filed 5 August 1999

GB 9927106.6, filed 16 November 1999

GB 0007637.2, filed 29 March 2000, and

PCT/GB00/01857, a PCT patent application filed at the United Kingdom Patent Office on Monday, May 15, 2000, claiming priority from the six UK patent applications.

A previous amendment to claim 12 added the limitation "at a dose level of about 500 to about 1650 micrograms/m^2 body surface area" which finds support in the specification on page 13 and in PCT/GB00/01857 on page 13. However, no clear support for this newly inserted dosage range is found in the prior-filed, non-US patent applications. As such, the earliest effective U.S. filing date afforded the instant claims is May 15, 2000.

Applicants point out GB 9911183.3, filed on 13 May 1999, GB 9911346.6, filed 14 May 1999, and GB 9927106.6, filed 16 November 1999, provide support for a dosage of 1500 μg/m^2. Further, GB 9918534.0, filed 5 August 1999, provides support for a dosage of 1650 μg/m^2.

As previously stated, no clear support for the dosage range "about 500 to about 1650 micrograms/m^2 body surface area" is found in the prior-filed, non-US patent applications. As such, the earliest effective U.S. filing date afforded the instant claims with respect to this recited claim limitation is May 15, 2000.

In the last Office Action claims 12-17 and 24-35 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of copending Application No. 10/492320. Claims 12-17 and 24-35 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No. 10/579251.

Applicants choose to hold these issues in abeyance. Accordingly, these provisional rejections on the ground of nonstatutory obviousness-type double patenting are maintained.

Claims 12-17 and 24-35 were rejected under 35 U.S.C. 112, second paragraph, in the last Office Action as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. It was asserted the metes and bounds of the term "about" cannot be precisely determined and should be deleted. The recitation in claim 12 "at a dose level of about 500 to about 1650 micrograms/m2 body surface area" was cited as exemplary.

While the term "about " has been deleted from claim 12, with respect to dosage ranges, the term remains in the other rejected claims of record. Accordingly, the rejection is maintained over claims 13-17 and 24-35.

Applicant's arguments with respect to claims 12-17 and 24-35 that were rejected under 35 U.S.C. 103(a) in the last Office Action, as being unpatentable over both Taamma et al., Eur. J. Cancer, and Cvitkovic et al., ASCO Meeting, view of Goodman & Gilman., have been considered and are persuasive.

Applicants argue the Citkovic reference is not available as prior art against at least some of the claims. Further, Applicants refer to the Declaration of Jose Jimeno under 35 U.S.C. § 1.131 and urge the listed co-authors of the Cvitkovic article, who are not listed as co-inventors, either did not arrive at the subject matter relied upon in the Office Action or were working under the direction of one or more of the listed co-authors/co-inventors.

With respect to the dosage 1500 $\mu g/m^2$, the prior-filed, non-U.S. patent applications provide clear support. Further, GB 9918534.0, filed 5 August 1999, provides support for a dosage of 1650 $\mu g/m^2$. However, no clear support for the dosage range "about 500 to about 1650 micrograms/m^2 body surface area" is found in the prior-filed, non-US patent applications. As such, the earliest effective U.S. filing date afforded the instant claims with respect to this recited claim limitation is May 15, 2000.

In view of the Declaration of Jose Jimeno under 35 U.S.C. § 1.131, and according to MPEP 715.01, Applicants have overcome the rejection of record because Cvitkovic et al., ASCO Meeting held May 17, 1999, (Abstract), published in Clinical

Cancer Research and on-line at www. asco.org., which was available as prior art under 35 U.S.C. 102(a), is presently unavailable because Applicants have declared that the subject matter relied upon in the reference was Applicants' own.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12-17 and 24-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over both Taamma et al., Eur. J. Cancer, and Riofrio et al., 23rd European Society for Medical Oncology Congress (abstract), in view of Goodman & Gilman.

Taamma teaches cyclic intravenous administration of Et-743 in the treatment of various solid tumors, such as breast or ovarian cancer, for an infusion time of 24 hours every 3 weeks. The patient population included those who were designated "refractory" to standard chemotherapy, and thus these patients, as required by claim 32, had previously been treated for cancer with chemotherapy. Riofrio teaches an ET-743 dosage range between 600-1800 mg/m^2, which encompasses the range recited in independent claim 12, to be administered as an intravenous infusion over 24 hours every 3 weeks to patients with solid tumors in advanced stages. Advanced stage tumors encompass metastatic disease. As required by claim 30, Riofrio includes such tumor types as colorectal, sarcoma, breast, ovary, renal, bladder, gastric, ACUP and

larynx. As required by claim 32, all patients were refractory to standard chemotherapy. As required by claims 34 and 35, see the Tables on page 930 in Goodman & Gilman, where dexamethasone is shown to be effective as an antiemetic in cancer chemotherapeutic regimens.

In view of the teachings of Taamma and Riofrio, one skilled in the oncology art would have been motivated to seek an optimal dosing regimen for ET-743 with respect to dosages, infusion times and intervals of administration through no more than routine experimentation. It is clear from the prior art that the determination of an optimal dosing regimen depends on tumor type, the stage at which a diagnosis is made, the presence or absence of metastasis, prior therapy, the over-all condition of the patient and the avoidance of adverse drug effects, such as thrombopenia, neutropenia, acute renal failure and transaminitis. Ample motivation to treat a human patient for cancer is provided for administering ET-743, optionally in combination with an additional drug, such as an antiemetic, with a reasonable expectation of success. Such determinations are within the purview of those skilled in the oncology art through no more than routine experimentation.

No claim is allowed.

Applicant's submission of an Information Disclosure Statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on July 16, 2007, prompted the new ground of rejection presented in this Office Action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this Final Action is set to expire THREE MONTHS from the mailing date of this Action. In the event a first reply is filed within TWO MONTHS of the mailing date of this Final Action and the Advisory Action is not filed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the Advisory Action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the Advisory Action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this Final Action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 4, 2007

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER

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